REMARKS

Applicant requests reconsideration of the aforementioned application in view of the foregoing amendments and the discussion below. The status of the claims is as follows: Claims 1-32 are pending and Claim 31 has been amended herein.

The Amendment

Claim 31 was amended to recite reacting the terminal hydroxy group of ascorbic acid with a protecting group and reacting the secondary hydroxy group of ascorbic acid with a protecting group. Claim 1 was also amended to indicate that the protecting group on the terminal hydroxy group is removed. Support for all of the above amendments is in the Specification, for example, Example 1.

Rejection under 35 U.S.C. §112

Claims 31 and 32 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant submits that the amendment to Claim 31 obviates this ground of rejection. Nonetheless, the paragraph at page 22, lines 9-15 provides an exemplary synthesis of an R-isomer of an NSAID as depicted in Fig. 1 by way of illustration and not limitation. Applicant submits that this language in the specification fully supports the original claim language of Claim 31.

Rejection under 35 U.S.C. §103

Claims 1-30 were rejected under paragraph (a) of the above code section as being unpatentable over Wechter, *et al.*, (U.S. Patent No. 5,981,592) (Wechter) in view of Zavitz, which was previously cited and applied.

Wechter discloses a composition for use in preventing colorectal cancer and other neoplastic diseases, such as breast cancer, that includes an enantiomerically stable R-NSAID or a pharmaceutically acceptable salt thereof in an amount effective to elicit a chemoprotective effect. The composition is substantially free of the S-enantiomer of the R-NSAID.

Wechter is devoid of any teaching of esters of R-NSAID's and Zavitz does not disclose or suggest the presently claimed ester compounds. Claim 1 and those claims depending therefrom recite that the esterifying agent comprises 3 to 6 carbon atoms, at least one hydroxyl group and one or more carboxyl groups or 1 to 4 hydroxyl groups or one or more aldehyde groups or a gamma lactone or a delta lactone or an amine or an imine or a lactam. The alkyl esters of Zavitz do not satisfy the definition of esterifying agent of the claims. Claim 7 recites that the esterifying agent comprises 3 to 6 carbon atoms, at least one hydroxyl group and one or more carboxyl groups and 1 to 4 hydroxyl groups. The alkyl esters of Zavitz do not satisfy the definition of esterifying agent of Claim 7 and those claims dependent therefrom. Claim 10 recites that the compound comprises one or more carboxyl groups and 1 to 4 hydroxyl groups. The alkyl esters of Zavitz do not satisfy the elements of Claim 10 and those claims dependent therefrom.

Zavitz does not disclose or suggest the presently claimed ester compounds as demonstrated above. The combined teaching of Wechter and Zavitz does not cure this deficiency since Wechter does not teach any esters. Furthermore, the conclusion that, since Zavitz teaches an equivalence of R-NSAID's and their esters in treating aids, one skilled in the art would be motivated to use esters of R-NSAID's taught by Wechter in the treatment is not warranted. The success of such imagined compounds as anti-cancer compounds would not be expected. Thus, even if for the sake of argument the skilled artisan would be so motivated, there would not be any reasonable expectation of success. At most, the situation would be one of obvious to try, which is not the standard for motivation under the statute. Furthermore, the combined teachings do not result in the presently claimed ester compounds as explained above.

Claims 1-6 and 10-32 were rejected under paragraph (a) of the above code section as being unpatentable over Wechter in view of Manfredini, which was previously cited and applied. Manfredini's disclosure relates to nipecotic acid, kinurenic acid and diclofenamic acid. These acids are not included in the definition of non-steroidal anti-inflammatory agent of the present claims.

The Office Action asserts that diclofenamic acid is an arylacetic acid and homologous to the arylpropionic acids of the present claims. Applicant disagrees. Diclofenamic acid

comprises two chlorine substituents.

Furthermore, even if for the sake of argument the skilled artisan would be motivated to combine the teachings of Wechter and Manfredini, there would not be any reasonable expectation of success. There is little reason that one skilled in the art would have to conclude that ascorbate esters of Wechter's compounds would be clinically effective. The skilled artisan would not have a reasonable expectation of a likelihood of success. As above, at most, the situation would be one of obvious to try, which is not the standard for motivation under the statute. Furthermore, Manfredini makes no disclosure relevant to other esterifying agents recited in the claims.

Claims 1-6 and 10-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Zavitz in view of Manfredini for essentially the reasons of record. The Office Action asserts that the former discloses the benefit of using the free acid as well as lower alkyl esters of NSAIDS in the R-form in the treatment of AIDS. Because of the disclosure of Manfredini concerning the pharmaceutical utility of using the ascorbates of certain drugs including an NSAID, argues the Office Action, the ascorbates of the R-NSAIDS of Zavitz would have been obvious to one of ordinary skill in the art.

Even if for the sake of argument the skilled artisan would be motivated to combine the teachings of Wechter and Manfredini, there would not be any reasonable expectation of success. As above, at most, the situation would be one of obvious to try, which is not the standard for motivation under the statute. There is little reason that one skilled in the art would have to equate ascorbate esters and simple C1-C6 alkyl esters as to their effectiveness in treating AIDS. The skilled artisan would not have a reasonable expectation of a likelihood of success. Furthermore, Manfredini makes no disclosure relevant to other esterifying agents recited in the claims.

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable, for essentially the reasons of record, over Zavitz in view of Alper, which was cited and applied previously. Alper discloses a process for the asymmetric production of carboxylic acid esters and/or carboxylic acids. The process comprises reacting a prochiral olefinic function and an alcoholic function or water with carbon monoxide, a single enantiomer of an optically active compound such as menthol, tartaric acid, tartaric acid ester, sugars, proteins and polypeptides, enzymes

and chiral phosphines and a catalyst.

The Office Action contends that Alper's disclosure of his method for preparing carboxylic acid esters combined with the teaching of Zavitz results in the presently claimed invention of Claims 1-30. However, one of the esterifying agents specifically claimed in the present application is tartaric acid. Since Alper employs an optically active tartaric acid or tartaric acid ester in his method, one skilled in the art would not reasonably look to Alper for any teaching that is combinable with Zavitz to produce the presently claimed compounds. Furthermore, it would be reasonable for the skilled artisan to conclude that Alper actually teaches away from the present invention. Accordingly, one skilled in the art would not have the requisite motivation for making the combination of teachings of the references suggested in the Office Action.

In reply to Applicant's comments above, the Office Action contends that Alper uses tartaric acid as an enantiomeric director and not as an esterifying agent. Applicant wishes to point out that the only esterifying agents disclosed by Alper are essentially alkanols. There is no disclosure regarding the esterifying agents of the present claims. Furthermore, Alper utilizes both an alkanol and tartaric acid or tartaric acid ester in his method. This is further evidence that Alper did not contemplate tartaric acid as one of his esterifying agents. As noted in the Office Action, tartaric acid is employed as an enantiomeric director and does not interfere with the preparation of the alkanol esters of Alper. Accordingly, as mentioned above, one skilled in the art might readily view Alper's disclosure as teaching away from the esterifying agents, such as, e.g., tartaric acid, employed by Applicant. Consequently, Alper cannot be viewed as disclosing anything relevant to the presently claimed ester compounds.

Claims 1-30 were rejected under 35 U.S.C. 103(a) as being unpatentable over Wechter in view of Zavitz and Alper for essentially the reasons of record. The Office Action previously asserted that Wechter and Zavitz are used to show the desirability of using R-esters of NSAIDS and that Alper shows how to make them and the optically active esters of NSAIDS with polyhydric alcohols.

For reasons similar to those discussed above with respect to the rejection over Wechter in view of Zavitz and Zavitz in view of Alper, the combined teachings of Wechter, Zavitz and Alper do not suggest the presently claimed inventions.

Conclusion

Claims 1-32 satisfy the requirements of 35 U.S.C. §§112 and 103. Allowance of the above-identified patent application, it is submitted, is in order.

Respectfully submitted,

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